

### **REMARKS**

The Office Action dated July 14, 2005, has been carefully reviewed. The Examiner maintains that the effective filing date of the instant application is August 1, 1995.

Claim 19 stands rejected as allegedly obvious double patenting of claims 37 – 58 of U.S. Patent No. 5, 334, 640.

Claim 19 stands rejected under 35 U.S.C. § 102 (b and e) as allegedly anticipated by Nisshinbo Industries Inc. EP 0 555 980, Sumino et al. 4, 791,061, Feijen, US 5,041,292 or Kobayashi et al. U.S. 5,268, 286.

Claim 19 also stands rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Desai, et al. (U.S. 5,550,178), Soon-Shiong, et al. (U.S. 5,705,270), Soon-Shiong, et al. (U.S. 5,700,848), Gunther, et al. (U.S. 5,736,595), Soon-Shiong, et al. (U.S. 5,837,747), Soon-Shiong, et al. (U.S. 5,846,530), or Mathiowitz, et al. (U.S. 5,985,354).

Applicants have amended claim 19 and added new claim 37 in order to more distinctly claim the subject matter of the invention. The claims are fully supported by the Application as filed.

.Reconsideration of this Application is respectfully requested in view of the foregoing amendments and additional remarks which have addressed all the grounds for rejection or have rendered them moot.

**The Examiner's basis for asserting that the earliest priority support for Claim 19 is August 1, 1995, instead of February 28, 1992, is clearly erroneous**

The patentability of claim 19 turns on what is deemed its earliest priority date. Whereas the Examiner asserts that it is August 01, 1995, Applicants contend that it is at least February 28, 1992.

In the prior Office Action, the Examiner erroneously alleged that U.S. Patent Applications 07/970,540 (abandoned), 07/958,870 (U.S. 5,529,914), 08/022,687 (U.S. 5,410,016), 08/336,393 (U.S. 5,820,882) and 08/379,848 (U.S. 5,626,863) do not

contain any subject matter regarding a biocompatible mixture containing at least one ionically crosslinkable component and at least one covalently crosslinkable component.

Applicants respectfully traversed and provided the Examiner with Exhibit 1 (herein resubmitted) setting forth the elements of claim 19, and an unbroken chain of support dating back to at least February 28, 1992.

In the current Office Action, the Examiner asserted that explicitly recited support for claim 19 is missing and in reference to Example 16 of U.S. 5, 626, 863, stated that said example has two ingredients reacting with each other instead of forming a mixture and the ingredients while being species of an ionically crosslinkable and a covalently crosslinkable component respectively, do not support a claim embracing two entire genera. Applicants respectfully submit that Exhibit 1 is explicit, clear, concise and convincing. It appears that the Examiner is looking for a literal phraseology rather than considering the underlying science and ample illustrations which clearly convey said unbroken chain of support for claim 19 dating back to at least February 28, 1992.

Applicants now ask the Examiner to consider Figures 1A to 1J herewith submitted for the Examiner's convenience. The same illustration is variously reproduced along the continuity chain and may be found, among other places, as Figure 1 of U.S. Patent No. 5, 626, 863 filed January 27, 1995 which claims priority to U.S. Serial No. 843,485 filed February 28, 1992. Said Figure 1 also appears as Figure 1 of U.S. 5,410, 016, filed Mar. 01, 1993 which claims priority to U.S. Serial No. 598,880 filed August 05, 1991. Said Figure 1 also appears as Figure 1 of U.S. Serial No. 09/910,663 (published as US 2003/0087985) filed July 19, 2001, which claims earliest priority to U.S. Serial No. 07/598,880, filed October 15, 1990.

**The Basic Science of the Macromer Exemplified by Figures 1A to 1J shows macromers having at least one Covalently Crosslinkable Component and at least one Ionically Crosslinkable Component**

Figures 1A to 1J are schematics of the macromers of the present invention. All the macromers illustrated have at least one photopolymerizable component. Also, all the macromers illustrated have at least one water-soluble component or one hydrolizable component or one water-soluble and hydrolizable component.

### **The Photopolymerizable Components of the Macromers are Covalently Crosslinkable**

The specification of the instant invention is replete with enabling descriptions, at the level of one of ordinary skill in the art, of how to attain photopolymerization of the macromers. The Examiner is particularly referred to column 9, lines 5-65, of U.S. 5,416,016, one of the patents in the priority chain for a basic description of the photopolymerization. There it was mentioned that:

The polymerizable regions are preferably polymerizable by photoinitiation by free radical generation.... The preferred polymerizable regions are acrylates, diacrylates, oligoacrylates ... and other biologically acceptable photopolymerizable groups. U.S. 5, 410, 016, Column 9, lines 5-18.

Likewise, the instant invention states rather explicitly that the photopolymerizable component is a side chain such as acrylate. US 2004/0138329, paragraph 0039. To that extent, one of ordinary skill in this art area understands that the photopolymerizable component of the macromers of the present invention is covalently crosslinkable. The fact that the Applicants did not originally characterize their macromers with terms having no more than aesthetic appeal does not detract in anyway from the fundamental chemical and physicochemical nature of their invention.

**The Water Soluble (e.g. PEG) or hydrolizable (e.g. polyglycolide) or water-soluble and hydrolyzable component (e.g. hyaluronate) are ionically crosslinkable**

One of ordinary skill in the art will appreciate that polyanions or polycations or polysaccharides will be ionically crosslinked by introduction of species having opposite charges. Thus, in the event that a substance such as alginate or hyaluronic acid is used as part of the macromers of this invention, the resulting macromers will be both ionically crosslinkable and covalently crosslinkable. U.S 2004/0138329 paragraph 0102. Thus, as shown in Figures 1A to 1J, the macromers of this invention contain at least one covalently crosslinkable component and at least one ionically crosslinkable component.

**The Examiner's insistence that Applicants Adopt Usage of Terms which have become popular in the art is in manifest error**

Applicants' main assignment of error on the Examiner's part is the failure to recognize the fundamental physical and chemical properties of the macromers of the present invention due to the Examiner's unjustified reliance on popular language that has evolved as the art area has evolved.

Basically, the Examiner is insisting that the terms "ionically crosslinkable" and "covalently crosslinkable" should have been explicitly used relating all the way back to the earliest priority date of the application. Applicants respectfully disagree. Applicants failure to characterize their invention using trendy language is not fatal. There is no requirement in law that priority must turn on recitations of terms which are later deemed popular or aesthetically preferable. The ionic and covalent crosslinkability of the macromers of the instant invention are fundamental as a matter of fact on their chemical properties. The Applicant's right to exclude infringers and subsequent inventors should not be diluted by the lexicographic preferences of putative infringers. The Applicant's right to their invention by any other name should be undisturbed and it is on that basis that the Applicants ask the Examiner to reconsider the priority chain submitted by the Applicant and grant the instant invention a priority dating back to at least February 28, 1992.

### **Double-Patenting Rejection**

Claim 19 stands rejected as allegedly unobvious double patenting of claims 37 – 58 of U.S. Patent No. 5, 334, 640. Applicants disagree.

The earliest priority date of the 5,334, 640 patent is April 08, 1992. Also, there are no claims 37-58 in said U.S. patent. Applicants respectively ask that this ground for rejection be withdrawn.

#### **Rejection under 35 U.S.C. § 102 (b):**

Claim 19 stands rejected under 35 U.S.C. §102(b) as being anticipated by Nisshinbo Industries Inc. EP 0 555 980, Sumino et al. 4, 791,061, Feijen, US 5,041,292 or Kobayashi et al. U.S. 5,268, 286. Applicants respectfully traverse.

In order for a reference to be a proper 35 U.S.C. §102(b) prior art reference, the invention must have been “patented or described in a printed publication in this or a foreign country . . . more than one year prior to the date of the application for patent.” The Nisshinbo reference was first published on August 18, 1993 and was patented on October 23, 1996. The instant application has an effective filing date, at the latest, of February 28, 1992, which pre-dates the Nisshinbo reference. Therefore, the Nisshinbo reference is not prior art and cannot anticipate the instant application.

Also, the Sumino et al. 4.791,061 reference does not teach the use of a macromers of the sort described above and exemplified by Figures 1A- 1J. The use of acrylamide and alginic acid monomers to carry out microbial entrapment is patentably distinct from the use of macromers having covalently and ionically crosslinkable components.

Likewise, Feijen et al. teaches a biodegradable hydrogel matrix useful for the controlled release of pharmacologically active agents formed by cross-linking a proteinaceous component and a polysaccharide or mucopolysaccharide, and then loading a selected drug therein.

Again, Feijen does not teach a macromer having a covalently crosslinkable and an ionically crosslinkable component. There is no basis for anticipation in this case and Applicants ask that this ground for rejection be withdrawn as well.

Likewise, Kobayashi teaches a biocatalyst immobilized with a graft product of a polymer and saponified polyvinyl acetate containing a stilbazolium group as a photo-crosslinking group. The polymer is preferably gelatin, collagen, starch, cellulose, gum arabic, tragacanth gum, carrageenan, mannan, dextrin or alginic acid. The graft product is prepared by bonding the polymer to the polyvinyl acetate, either directly through functional groups of the polymer and polyvinyl acetate or through a crosslinking agent.

Kobayashi does not teach a macromer having both an ionically and a covalently crosslinkable component. For that at least, there is no basis for anticipation and Applicants ask that this ground for rejection be withdrawn as well.

**Rejection under 35 U.S.C. § 102(e):**

Claim 19 stands rejected under 35 U.S.C. § 102(e) as being anticipated by Desai, et al. (U.S. 5,550,178), Soon-Shiong, et al. (U.S. 5,705,270), Soon-Shiong, et al. (U.S. 5,700,848), Gunther, et al. (U.S. 5,736,595), Soon-Shiong, et al. (U.S. 5,837,747), Soon-Shiong, et al. (U.S. 5,846,530), or Mathiowitz, et al. (U.S. 5,985,354). Applicants respectfully traverse.

The references cited by the Examiner are all patents and therefore fall under 35 U.S.C. §102(e)(2). In order for a reference to be a proper 35 U.S.C. §102(e)(2) prior art reference, the invention must have been described in . . . “a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for the purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language. However, references based on international applications that

were filed prior to November 29, 2000 are subject to the former (pre-AIPA) version of 35 U.S.C. §102(e) as set forth below. MPEP §706.02(a).

Former 35 U.S.C. §102 (e): “A person shall be entitled to a patent unless . . . the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.” See MPEP §706.02(a).

Patents issued directly, or indirectly, from international applications filed before November 29, 2000, may only be used as prior art based on the provisions of 35 U.S.C. 102(e) in effect before November 29, 2000. Thus, the 35 U.S.C. 102(e) date of such a prior art patent is the earliest of the date of compliance with 35 U.S.C. 371 (c)(1), (2) and (4), or the filing date of the later-filed U.S. continuing application that claimed the benefit of the international application. MPEP §706.02(a).

International applications, which were filed prior to November 29, 2000, may not be used to reach back (bridge) to an earlier filing date through a priority benefit claim for prior art purposes under 35 U.S.C. §102(e). MPEP §706.02(a).

Soon-Shiong, et al. Patents:

Since the four Soon-Shiong, et al. patents (U.S. 5,700,848; 5,705,270; 5,837,747; 5,846,530) issued directly, or indirectly, from an international application (PCT/US92/09364; filed October 29, 1992) filed before November 29, 2000, the pre-AIPA 35 U.S.C. §102(e) applies. As such, the earliest effective filing dates for the three Soon-Shiong patents listed above would be October 29, 1992 based on the 35 U.S.C. §371 compliance date. Although the international application claims priority to a CIP application (U.S. application 07/784,267; filed October 29, 1991), the four above-listed patents cannot use the international application to bridge the gap. MPEP 706.02(a). Since the instant application has an effective filing date, at the latest, of February 28, 1992, which is prior to the four Soon-Shiong, et al. patents' effective

filing date, they are not prior art and therefore cannot anticipate the instant application.

*Gunther, et al. Patent:*

With respect to the Gunther, et al. patent (U.S. 5,736,595), it would be treated the same way as the Soon-Shiong patents because it is a patent based on an international application filed before November 29, 2000. Since, the pre-AIPA 35 U.S.C. §102(e) would apply, the effective filing date for the patent would either be the filing date in the United States or when the 35 U.S.C. §371 requirements were met. The Gunther, et al. patent has a 35 U.S.C. §371 date of November 3, 1995, which is also the 35 U.S.C. §102(e) date, which is after the effective filing date for the instant application. Therefore, the Gunther, et al. patent is not prior art and thus, cannot anticipate the instant application.

*Desai, et al Patents and Mathiowitz, et al. Patent:*

With respect to the Desai, et al patents (5,550,178) and Mathiowitz, et al. patent (U.S. 5,985,354), the proper 35 U.S.C. §102(e) to use would be the current statute. Thus, the effective date for the Desai, et al. patents is April 8, 1992 (the application filing date and earliest claim to priority) and the effective date for the Mathiowitz, et al. patent is June 7, 1995 (the application filing date). Since both effective filing dates for 35 U.S.C. §102(e) purposes are after the effective filing date of the instant application, the three patents are not prior art. Therefore, the three patents cannot anticipate the instant application.

Applicants respectfully request reconsideration and withdraw of this ground of rejection because the cited patents are not prior art and thus, cannot and do not anticipate the instant application.

**CONCLUSION**

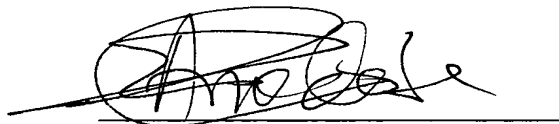
All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding



Office action and, as such, the present application is in condition for allowance. Applicants wish to expedite the prosecution process and if the Examiner believes, for any reason that personal communication will help expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Response is respectfully requested.

Respectfully submitted,  
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# EXHIBIT 1

Our Ref.: 354848-20001 Pending Claims of U.S. 10/43,687	Support Within 08/510,089 Application's Specification (08-01-95) CPAs (05-19-98 & 01-28-00)	Support Within 08/275,848 (U.S. 5,626,853) Application's Specification (01-27-96)	Support Within 08/022,887 (U.S. 5,410,016) Application's Specification (03-01-93)	Support Within 07/843,455 Application's Specification (02-28-92)	Support Within 07/558,370 (U.S. 5,529,914) Application's Specification (10-07-92)	Support Within 07/570,540 Application's Specification (04-20-92)	Support Within 08/336,393 (U.S. 5,820,892) Application's Specification (11-10-94)
19. A crosslinkable biocompatible mixture comprising:	page 11, lines 16-18; page 13, lines 15-20; page 18, line 7; page 28, line 24-26; Ex. 18, page 69	column 3, lines 65-67; column 4, lines 12-14; column 4, line 63 to column 5, line 4; column 5, lines 58-60; column 7, lines 47-50; Ex. 11, column 20, line 61 to column 21, line 15; Ex. 12, column 21, line 15 to column 25, line 22	column 4, lines 14-17 and 28-31; column 5, lines 15-23; column 6, lines 11-16; column 8, lines 8-12; Ex. 11, column 21, lines 47-49; Ex. 12, column 22 to column 26, line 17	page 15, lines 9-12; page 20, lines 30-35; page 22, lines 15-18 and lines 28-32	column 5, lines 42-44; column 6, lines 12-17; column 7, lines 25-27; column 13, lines 15-27; Ex. 10, column 19	page 12, lines 5-10; page 13, lines 6-14; page 21, line 18 to page 22, line 9; Ex. 10, page 33	column 4, lines 37-39; column 5, lines 82-85
at least one ionically crosslinkable component; and	page 30, lines 8-12; page 31, lines 8-18; page 130, lines 5-21	column 8, lines 9-16 and 41-47; Ex. 16, column 26, lines 41-60	column 8, lines 40-48; column 9, lines 6-13; Ex. 16, column 27, lines 31-52	page 16, lines 18-22; page 27, lines 2-5	column 11, lines 19-28	page 18, lines 11-22; page 21, lines 5-17	column 4, line 44, 48, 50-51; column 5, lines 48, 50-52
at least one covalently crosslinkable component,	page 28, line 15 to page 30, line 20; page 31, lines 8-29; page 32, line 1 to page 37, line 18; page 92, line 25 to page 104, line 14; page 130, lines 5-21; Figs. 1, 2, 3	column 8, lines 9-16 and 41-47; Ex. 16, column 26, lines 41-60	column 8, lines 40-48; column 9, lines 6-13; Ex. 16, column 27, lines 31-52	page 13, lines 6-10; page 15, lines 8-24; page 16, lines 16-22; page 20, lines 15-20; page 24, lines 18 to page 25, line 2; page 26, line 33 to page 27, line 11; Fig. 1	column 11, lines 19-28	page 16, lines 23-28; page 18, lines 11-22; page 21, lines 5-17	column 4, line 44, 48, 50-51; column 5, lines 48, 50-52; column 6, lines 1-3; claim 2 and claim 3
wherein the ionically crosslinkable component is selected from a polysaccharide, a polyanion, or polycation.	page 28, line 15 to page 30, line 20; page 31, lines 8-29; page 87, line 5 to page 88, line 13; page 130, lines 5-21	column 8, lines 9-16 and 41-47; Ex. 15, column 26, lines 15-38; Ex. 16, column 26, lines 41-60	column 8, lines 40-48; column 9, lines 6-13; Ex. 15, column 27, lines 6-30; Ex. 16, column 27, lines 31-52	page 16, lines 18-22; page 26, line 33 to page 27, line 11	column 11, lines 19-28	page 16, lines 23-28; page 18, lines 11-22; page 21, lines 5-17	column 4, lines 42-54; column 5, lines 42-45; column 6, lines 15-21; claim 7